4:27:53 OCA PAD INITIATION - PROJECT HEADER INFORMATION 08/05/87

Project # E-25-M23_____ MOD # _____ REV # 0__
Contract # 1 R29 HL39437-01_____ OCA file # ___ Status A
Contract entity GTRC Prime contract # _____
PDPI KU D N_____ (
SSN - - Unit ME Phone ( ) -
Project unit ME_____ Unit code 02.010.126
Sponsor/Division DHHS/PHS/NIH /NHLBI / NATL INSTITUTE OF HEALTH_
Sponsor#/division # 108 / 001
Type of document GRANT__
Award period: from 87 / 08 / 01 to 88 / 07 / 31 (perf) 88 / 10 / 31 (rpts)

Sponsor amount	New this change	Total to date
Contract value	$ 101076	101076
Funded	$ 101076	101076

Cost sharing # _____ Cost sharing $ _____
Does subcontracting plan apply? (Y/N) N
Title -
HUMAN ATHEROSCLEROSIS: ROLE OF PULSATILE FLOW_____

CTR project # R6357-0A0_____ CTR cost sharing # _____

Are there existing subprojects? (Y/N) N
Is this a subproject? (Y/N) N Main project # _____
Continuation of project # _____ Type of research RES____

Coproject director name

_____
SSN - - Unit

Coproject director name

_____
SSN - - Unit
PAD login date 87/08/05
PAD process complete date 87/08/05

PROJECT ADMINISTRATION DATA

Administrative data OCA contact E. FAITH GLEASON____ PAD CO EFG 894-4820

Sponsor technical contact	Sponsor issuing office
DR. EDWIN C. GANGLOFF_____	JANE R. DAVIS_____
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DIV OF HEART & VASCULAR DISEASES____	DIV OF EXTRAMURAL AFFAIRS_____
NAT HEART, LUNG, & BLOOD INST_____	NAT HEART, LUNG, & BLOOD INST_____
BETHESDA, MD 20892_____	BETHESDA, MD 20892_____

Security class (U,C,S,TS) __ ONR resident rep. is ACO (Y/N) N
Defense priority rating N/A___
_____ supplemental sheet
Equipment title vests with Sponsor _ GIT X Comment follows -

Admin comments -
INITIATION. SUPPORT HAS BEEN RECOMMENDED FOR FIVE YEARS._____

GEORGIA INSTITUTE OF TECHNOLOGY OFFICE OF CONTRACT ADMINISTRATION

SPONSORED PROJECT TERMINATION/CLOSEOUT SHEET

Date 10/26/88

Project No. E-25-M23 / 246R63570A0 School/~~Lab~~ ME

Includes Subproject No.(s) N/A

Project Director(s) D. N. Ku ~~GTRC~~/GIT

Sponsor DHHS/PHS/NIH/NHLBI National Institute of Health

Title Human Atherosclerosis: Role of Pulsatile Flow

Effective Completion Date: 7/31/88 (Performance) 10/31/88 (Reports)

Grant/Contract Closeout Actions Remaining: NOTE: Annual report submitted with continuous proposal.

- [ ] None
- [XX] Final Invoice or Copy of Last Invoice Serving as Final
- [ ] Release and Assignment
- [ ] Final Report of Inventions and/or Subcontract:
  Patent and Subcontract Questionnaire sent to Project Director [ ]
- [ ] Govt. Property Inventory & Related Certificate
- [ ] Classified Material Certificate
- [ ] Other

Continues Project No. Continued by Project No. E-25-M62

COPIES TO:

Project Director
Research Administrative Network
Research Property Management
Accounting
Procurement/~~GTRI Supply Services~~
~~Research Security Services~~
Reports Coordinator (OCA)
Program Administration Division
Contract Support Division

~~Facilities Management - ERB~~
~~Library~~
~~GTRC~~
Project File
Other

8-25-4723

SECTION IV PROGRESS REPORT SUMMARY	GRANT NUMBER HL 39437-02	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR David N. Ku	PERIOD COVERED BY THIS REPORT FROM	THROUGH
APPLICANT ORGANIZATION Georgia Institute of Technology	08/01/88	07/31/89

TITLE OF PROJECT *(Repeat title shown in item 1 on first page)*
HUMAN ATHEROSCLEROSIS: ROLE OF PULSATILE FLOW

(SEE INSTRUCTIONS)

Objectives

Studies of the human carotid bifurcation indicate that atherosclerotic plaques form preferentially in regions of low and oscillatory shear stress. The proposed research is designed to define the hemodynamic determinants of plaque in the human abdominal aorta.

Specific Aims for next year of support

In the first year of this grant, we defined the average anatomy of the abdominal aorta and constructed a laboratory flow system. We have collected data as to the steady flow characteristics of flow in this model. In the second year, we will explore the pulsatile hemodynamic environment of the abdominal aorta using dynamic flow visualization techniques of dye injection and particle tracking. We will explore the importance of variations in geometry, branch flow division, and pulsatile waveform.

Experimental Design and Methods

Although it is our objective to provide a detailed flow description of hemodynamics in the abdominal aorta, selectivity is clearly required lest the number of measurements prove monumentally prohibitive.

We have constructed three models of the abdominal aorta including the branches to the celiac, superior and inferior mesenteric, renals, and iliac arteries. These models are based on the average dimensions from 55 biplanar aortograms of human subjects. A standard average model was constructed as well as two variations incorporating different branch angles and radius of curvature. These models will be used to identify the relative effects of these anatomic variations on the detailed hemodynamics in the aorta.

Due to changes in peripheral resistance, digestive requirements, and renal blood flow, the physiologic range of aortic branch flow divisions will be modelled. Three conditions will be consistently explored: rest, postprandial state, and exercise. The absolute pressure and pressure gradients in the test section will be measured using absolute and differential pressure transducers. From these measurements, the peripheral impedances can be calculated and controlled.

Ensemble averaged flow pulse waveforms will be used to drive the pulsatile flow in the thoracic aorta. Changes in pulse rate primarily affect the duration of diastole and hence the length of time for which flow is quasi-steady. A series of experiments will be performed in which the pulse rate in the standard bifurcation model is doubled, primarily by the sacrifice of diastolic time, in order to determine whether significant flow field changes occur.

During each cycle the abdominal aorta waveform frequently contains a period of negative flow which tends to heighten with inactivity and increased digestive requirements. We plan to study localized hemodynamic patterns under a range of physiological waveforms, using a range of deceleration slopes similar to those described for our previous the carotid studies.

The working fluid is a mixture of water and glycerin adjusted to yield an absolute viscosity of 0.035 g/cm/sec. The fluid is pumped from an upstream tank through an electronically controlled shaker valve/pulsatile pump into a straight tube 3 meters long. The input waveform is stored digitally on a programmable-read-only-memory (PROM) chip and may be easily altered to study the effect of flow waveform shape on modelled arterial hemodynamics. The mean Reynolds number for the thoracic aorta input is 500.

Flow visualization will be performed in one of three glass blown models of the abdominal aorta to establish a heuristic sense of the flow patterns as well as to identify regions of particular interest. Flow visualization is achieved by observing and

photographing hydrogen bubbles or colored dye injections in the flow Hydrogen bubbles are generated by applying a current of 0.5 mamp through a 0.0015 inch (0.038 mm) diameter stainless steel wire which is oriented in the plane of the bifurcation. Still photographs are taken sequentially using Kodak 2475 recording film or Ektachrome 160 slide film with a Canon AT-1 35 mm camera with a 55 mm macro lens. Movies are made with a JVC Model 555 Super VHS camcorder. The test section is illuminated from above and below by two quartz halogen spotlights.

No substantive changes have been made since the original grant proposal.

Progress report for current budget year

Carotid atherosclerosis develops in regions of low and oscillatory shear stresses. Similar hemodynamic factors may influence plaque formation in the abdominal aorta. The abdominal aorta is an important site of clinical atherosclerosis and is complex in that, not only is the hemodynamic behavior complicated due to the presence of several branches and a wide range of flow rates but, this vessel segment has two differing responses to disease: occlusive plaque formation and development of aneurysms. We are engaged in a study of the hemodynamics and lesion distribution of the abdominal aorta using flow models and morphometric evaluation of human specimens.

We have constructed a glass blown model of the abdominal aorta, including celiac superior and inferior mesenteric, renal and iliac branches, based on 55 biplanar angiograms from person ranging from 27-88 years. Forty-two parameters were measured from these angiograms including lengths, branch angles, diameters and radii of curvature. As an independent check, ten pressure - perfusion fixed cadaver specimens were obtained and analyzed for equivalent dimensions. Different physiologic states - such as rest, exercise, digestion - strongly influence the flow and flow divisions in this region. Mean values were estimated from data in the literature for rest and for exercise.

Under rest conditions, two regions of relative stagnation appeared on the posterior wall of the aorta. Secondary flow patterns appeared in the abdominal aorta, but not in the thoracic aorta. Under exercise conditions, one thin stagnation region appeared and no secondary flow patterns were visible. With pulsatile flow, the stagnation regions exhibited oscillatory motion. The secondary flow patterns became more complicated, but still appeared only in the abdominal aorta. These vortices propagated downstream during systole, with additional vortices forming in early diastole. For pulsatile exercise flow conditions, virtually no secondary flow patterns appeared. Results from this experiment show that complicated flow patterns exist locally in the abdominal aorta which may influence the development of plaque at this site.

This work has been presented at the Annual Conference in Medicine and Biology, 1987, the Winter Annual Meeting of the American Society of Mechanical Engineers, 1987, and is to be presented at the Annual Meeting of the International Society for Cardiovascular Surgery, 1988 and the World Congress on Bioengineering, 1988. A Master of Science thesis on this topic is available for inspection as is a manuscript entitled "Flow Patterns in the Abdominal Aorta under Simulated Postprandial and Exercise Conditions" is being prepared for the Journal of Vascular Surgery.